c. a third element, linked to and comprised in a separate polypeptide chain from said first and second elements, comprising a therapeutic element derived from a Clostridial neurotoxin able, when present in the cytoplasm of a pancreatic cell, to inhibit or block enzymatic secretion by said pancreatic cell, and wherein following binding of said first element to a pancreatic acinar cell said composition is transported across a pancreatic cell membrane.

REMARKS

Rejection of Claims 1-24 under 35 USC § 112(1)

Claims 1-24 are currently pending. The Examiner has rejected these claims as allegedly violating the enablement requirement of 35 USC § 112(1). While Applicants do not agree that the claims were lacking enablement in the specification, in the interests of achieving allowance of the present application claim 1 has been amended to indicate that the first element is able to specifically bind the CCK-A or CCK-B receptor, and believe that the resulting claims are clearly patentable.

The Examiner has rejected the claims because the claims are said to be enabled only for a binding element comprising SEQ ID NO:2-6. Applicants respectfully disagree.

The enablement requirement of 35 USC §112(2) requires that the specification show the person of ordinary skill in the art how to make and use the invention without requiring undue experimentation. The case law on the subject of enablement is clear: a patent "need not teach, *and preferably omits*, what is well-known in the art." *Spectra-Physics, Inc. v. Coherent, Inc.*, 3 USPQ2d 1737 (Fed. Cir. 1987) (quoting *Hybritech Inc. v. Monoclonal Antibodies Inc.*, 231 USPQ 81 (Fed. Cir. 1986) (emphasis added).

In the present case, the specification teaches 5 specific examples of the claimed binding element by amino acid sequence: SEQ ID NO:2-6 are exemplary of peptide binding elements that are able to bind the CCK-A or CCK-B receptors. However, the invention is not limited to fusion peptides containing one of these sequences, nor does the patent law require enablement of each and every embodiment of an invention. Rather, what is required under the law is that there be a reasonable relationship between the scope

of enablement and the claim.

Recently, the Court of Appeals for the Federal Circuit has directly addressed this issue in the context of specific cell surface binding moieties. In *Johns Hopkins University v. Cellpro, Inc.*, 47 U.S.P.Q.2d 1705 (Fed. Cir. 1998), the court held that deposit of a single hybridoma cell line containing a single monoclonal antibody provided sufficient teaching to enable one to make and use the genus of monoclonal antibodies specifically binding to the same antigen without undue experimentation. Moreover, the *Johns Hopkins* court quoted and cited with approval its earlier case law illustrating that a considerable amount of experimentation is permissible to comply with the enablement requirement, if it is merely routine. *Id.* at 1719 (citing *PPG Industries, Inc. v. Guardian Industries, Corp.*, 37 USPQ2d 1618, 1623 (Fed. Cir. 1996); *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Both *Johns Hopkins* and *In re Wands* dealt with enablement issues in the field of antibody production; both cases held that the skill in the field is high, that the amount of experimentation necessary is no bar to patentability, and that the techniques employed to raise antibodies, such as the Kohler/Milstein method cited in *Johns Hopkins*, are exceptionally well known in the art.

Similarly to the situation in *Johns Hopkins*, the presently claimed binding elements provide a guide to the person of skill in the art to find other binding moieties, both peptide and non-peptide, that are capable of binding to the CCK-A and CCK-B receptors. Foe instance, the exemplary compositions comprising SEQ ID NO: 2-6 can be used in competition experiments in screening, for example, compounds from a combinatorial library against pancreatic acinar cells for their ability to bind the CCK receptor(s). A large number of combinatorial libraries are commercially available, and the techniques used to make such libraries are well-known in the art. The level of skill in the art is high, and the amount of experimentation required merely routine.

Thus, the present claims are clearly enabled to the person of ordinary skill in the art by the specification, in light of what is well-known in the art, and Applicants therefore ask the Examiner to withdraw the rejection.

CONCLUSION

For the reasons given above, Applicants again respectfully urge the Examiner to reconsider rejection of the pending claims. If any fee is required in connection with this communication; please use Deposit Account 01-0885 for payment of any fee that may be due.

Respectfully submitted,

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MARKED-UP COPY OF AMENDED CLAIM

1. (4 times amended) A composition able to [for the] treat[ment of] acute pancreatitis in a mammal comprising,

a) a first element comprising a binding element able to specifically bind a CCK-A or CCK-B receptor [a pancreatic cell surface marker] under physiological conditions,

b) a second element comprising a translocation element derived from a Clostridial neurotoxin able to facilitate the transfer of a polypeptide across a vesicular membrane in a pancreatic cell, and

c) a third element, linked to and comprised in a separate polypeptide chain from said first and second elements, comprising a therapeutic element derived from a Clostridial neurotoxin able, when present in the cytoplasm of a pancreatic cell, to inhibit or block enzymatic secretion by said pancreatic cell, and wherein following binding of said first element to a pancreatic acinar cell said composition is transported across a pancreatic cell membrane.